Amino Acids

Introduction

We're going to mix it up and focus on amino acids, proteins, and explore them as they're enzymes that do things—either as the primary substrate or as a catalyst. We'll begin by going deeper into amino acids. Just to maintain consistency, we used the coding DNA strand, 5' to the left, 3' to the right. We made an mRNA strand that was that DNA strand, only U's for T's, 5' to the left, 3' to the right. Using rRNA ribosomes we translated that transcript and made an amino acid sequence, 5' to the left, 3' to the right, which actually means N-terminus to the left, C-terminus to the right. Let's drill down into the amino acid itself.

Amino Acid Structure

The α-carbon is the central carbon that bonds to everything. "Everything" consists of an amino group, a carboxyl group, a hydrogen, and a side chain.
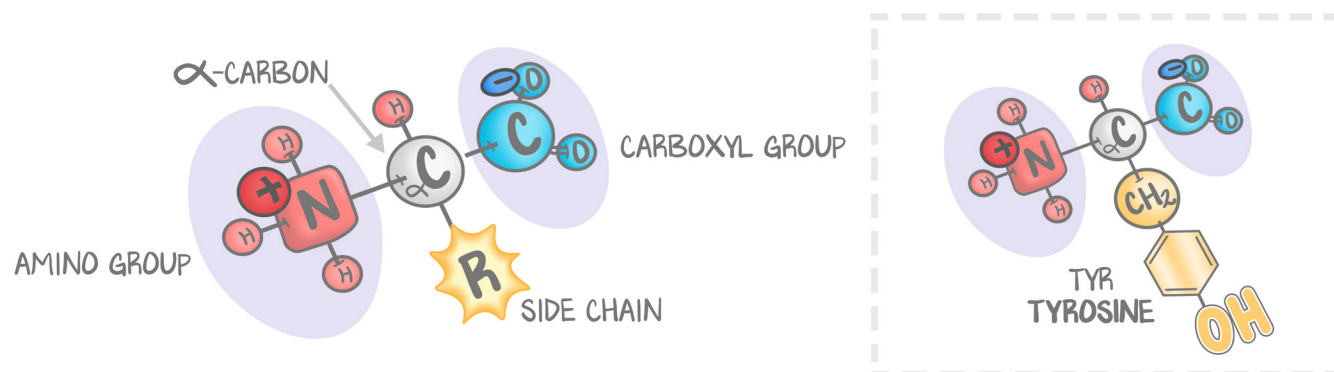

Figure 16.1: Amino Acid Structure
The α-carbon links all four subgroups. There is the amino group (nitrogen-containing in red), the carboxyl group (carbon-containing in blue), the hydrogen (in grey), and the variable side chain. The side chain defines the amino acid, and all amino acids have the same amino, carboxyl, hydrogen, and α-carbon.

The **amino group** is the nitrogen. At physiological pH, it exists as NH_3^+ with a positive charge. The **carboxyl group** is the carbon. The carboxyl group, at physiological pH, exists as COO^- with a negative charge. The whole molecule is neutral because the amino balances the carboxyl group at physiological pH (this can change based on the side chain, but before considering "R" the molecule is neutral).

The N-terminus of the growing peptide chain is the amino group of the first amino acid. The next amino acid connects its amino group to the carboxyl group of the last amino acid in the growing chain. To do that, the carboxyl group is attached to tRNA. **Peptide bonds** form between the amino group of an incoming amino acid and the carboxyl group of the old strand. The **hydrogen** is just that, it does nothing. All of these things are the same in all amino acids.

The **only difference between amino acids** is the **side chain**, which can be a whole host of different things. The side chain determines the amino acid, its hydrophobic or hydrophilic properties, and whether it carries a charge. Everything is in the side chain.

pH and pK

If we're not careful, we can get lost in this craziness. But it doesn't have to be challenging if you stay focused on solution.

pH refers to the **solution**, **pK** to the **amino acid** (and therefore, in conglomerate, the protein). Reference yourself from the solution. If the **pH is low**, there's a more acidic environment. More acid means more H^+ floating around. If the solution has too many H^+ (it's acidic), it'll want to get rid of H^+ by donating them. If the **pH is high**, it's a less acidic environment. Less acid means less H^+ floating around. If the solution has too few H^+ (it's alkalotic), the solution will want more of it and will accept H^+ from the protein.

A **low pH solution will donate H^+**, a **high pH solution will accept H^+**.

Notice we gave no reference of any kind. That's because when considering amino acids, the only thing we care about is the **pK of the amino acid**. Therefore, by the transitive property:

1.   If the pH of the solution is < the pK of the amino acid, the solution is more acidic, the solution has more H^+, and will donate H^+ to the amino acid.

2.   If the pH of the solution is > the pK of the amino acid, the solution is less acidic, the solution has less H^+, and will accept H^+ from the amino acid.
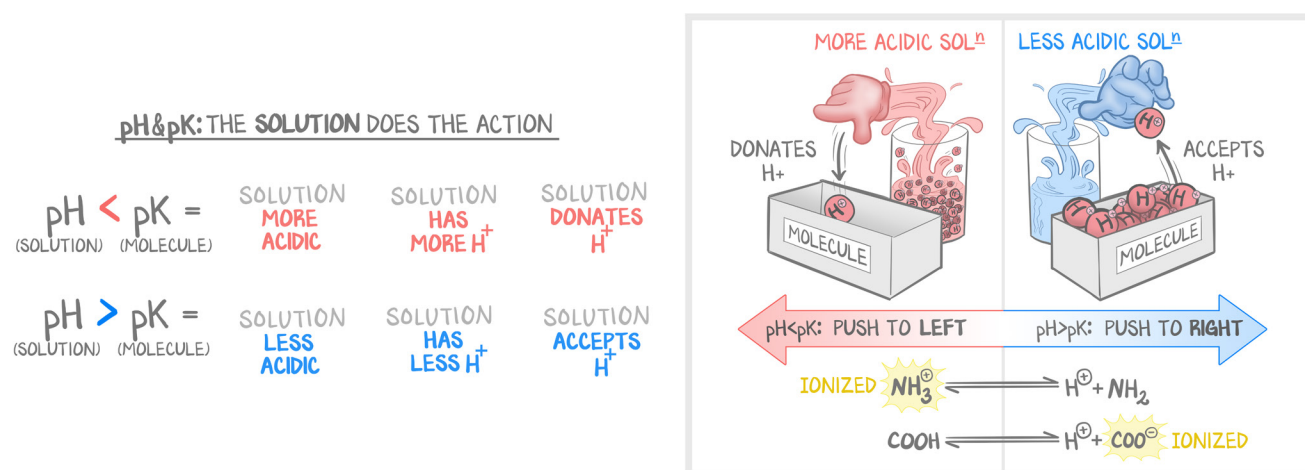

Figure 16.2: pH and pK
The solution does the giving or the taking, depending on the relative amount of hydrogens are around. If pH < pK, the solution donates to the group; if pH > pK, then the solution takes H^+ from the group.

The **pK changes** for **each group**. The pK of the carboxyl group is 2. The pK of the amino group is 9. Watch what happens.

NH_3^+ is the ionized form of the amino group, which happens when the solution donates the H^+ to the group. The pK for the amino group is 9. Physiological pH is 7.4. In this case, the pH is less than pK, the solution has more acid, has more H^+, and donates the H^+. The amino group can exist as either NH_3^+ **OR** $NH_2 + H^+$ . . . But the solution wants to donate H^+, so that pushes the reaction towards NH_3^+. Therefore, at physiological pH (7.4) the amino group exists as NH_3^+.

COOH is the unionized form, while COO^- is the ionized form. The pK for the carboxy group is 2. Physiological pH is 7.4. In this case, the pH is more than pK, the solution has less acid, has less H^+, and so accepts the H^+. The carboxyl group can exist as $COO^- + H^+$ **OR** COOH . . . But the solution wants to accept H+, so that pushes the reaction towards COO^-. Therefore, at physiological pH (7.4) the carboxyl group exists as COO^-.

As long as we compare the pH of the solution to the pK of the amino acid, and move the H^+ relative to the solution, no matter what pK or pH is presented, we'll be able to figure it out.

Amino Acid Categorization: Hydrophobic/Lipophilic

There are two major categories: hydrophobic and hydrophilic.

Hydrophobic means "doesn't like water" because it **isn't charged** or **polar**. Hydrophobic, by definition, means lipophilic. These amino acids are those that might be found **within a cell membrane** as in a transporter or simply a lipophilic domain of a transmembrane protein. This might be the target of the signal sequence that directs the ribosome to the ER. Hydrophobic/lipophilic amino acids are further broken down into **aromatic** (rings) and **aliphatic** (no rings).

In the **aliphatic**, notice the progression from glycine to isoleucine. It basically just keeps adding carbons. The chain gets longer left to right (we did that on purpose). The proline does its own thing and is Pr-whoa-line. Also notice that the progression goes from simple glycine to more complicated isoleucine. The most complicated are **essential amino acids**. We can't make them; they must be ingested (eaten). But imagine how easy it would be to remove stuff to get back to alanine. We can make alanine from the ingested, more complicated amino acids.

In the **aromatics**, there are only three to know. **Phe** is **just a ring**. **Trp** is **ring + ring**. Neither of these can be made; they're essential amino acids. **Tyr** is Phe with an –OH stuck onto it. Look for the **rings** to help decide if aromatic or not.
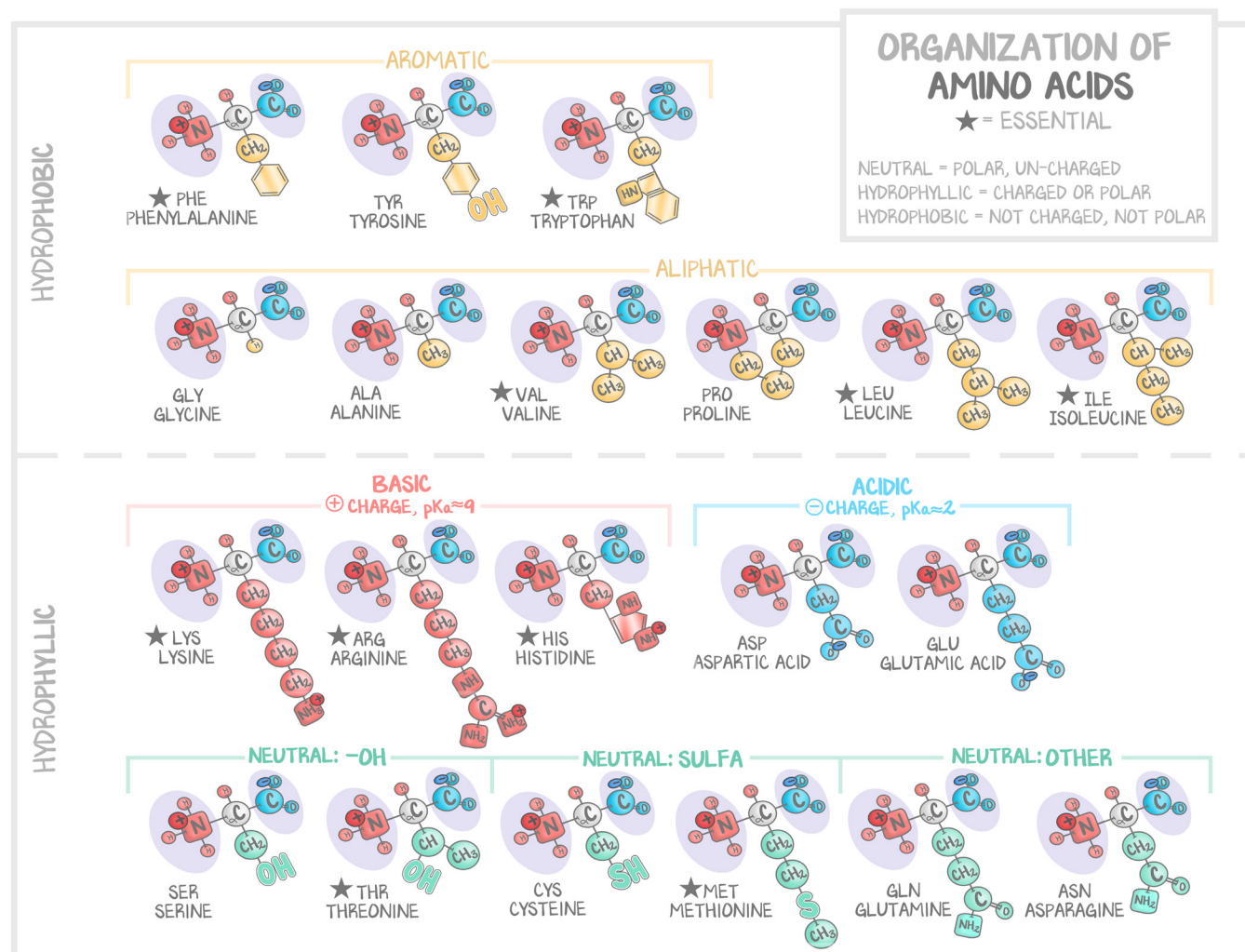

Figure 16.3: Amino Acids
Categorized and color-coded for easy memorization.

Amino Acid Categorization: Hydrophilic/Lipophobic

Hydrophilic means "likes water" because it's either **polar** or **charged**. Hydrophilic, by definition, means lipophobic. These amino acids like being in **cytoplasm** or to be **exposed extracellularly**. They **don't pass** through membranes well. They work intracellularly or intravascularly, or are surface proteins, or get excreted. There are three categories: **positive-charged**, **negative-charged**, and **polar but uncharged**.

Positive-charged amino acids get that way because they have an extra NH_3^+ in their side chain. Because the pK of NH_3^+ is 9, and the physiological pH is 7.4, the solution is less than pK, which means it is more acidic, has more H^+, and so will donate. That pushes the equation towards NH_3^+. And because these amino acids have TWO NH_3^+ and ONE COO^- total, the net charge is **+1**. Histones interact with DNA via their positive amino acids with the negative phosphate-pentose backbone. Histones are pushed towards euchromatin by **acetylating lysine**. Lysine is a positively charged amino. By acetylating it, its positive charge was removed. **ALL THREE** positive-charged amino acids (Lys, Arg, His) are **essential amino acids**.

Negative-charged amino acids get that way because they have an extra COO^- on their side chain. There are only two of them (Asp and Glu). We'll let you run through the exercise if you want to, but won't force people to read it again. The net charge is **-1** because there are **TWO COO$^-$** and one NH_3^+.

Polar but not charged has the least consistency of any group. It has three subgroups, -OH (hydroxyl), -S (sulfa), and Amino (H_2N-C=O). The **hydroxyls** are serine and threonine. The more complicated one, Thr, is an essential amino acid. They can be the target of O-glycosylation in the Golgi. The **sulfas** are cysteine and methionine. The more complicated one, Met, is an essential amino acid. Aspartate and glutamate are left over; we lump them in with proline—there is no pattern, simply memorize.